ROBERT D. MCCALLUM, JR.
Assistant Attorney General
Civil Division
EUGENE M. THIROLF
Director
Office of Consumer Litigation
GERALD C. KELL
Senior Trial Counsel
Office of Consumer Litigation
ALAN PHELPS
Trial Attorney
Office of Consumer Litigation
U.S. Department of Justice
P.O. Box 386
Washington, D.C. 20044
Tel: (202)307-6154

Attorneys for the United States

IN THE UNITED STATES DISTRICT COURT
FOR THE CENTRAL DISTRICT OF CALIFORNIA

IN RE PAXIL LITIGATION	NO. CV 01-07937 MRP (CWx) BRIEF OF THE UNITED STATES OF AMERICA
THIS DOCUMENT RELATES TO ALL ACTIONS	

Pursuant to this Court's instruction, the United States of America, on behalf of the United States Food and Drug Administration (FDA), hereby submits this brief detailing the issues related in its Statement of Interest regarding the Court's Memorandum of Decision re Preliminary Injunction filed on August 16, 2002.

As the factual statements below and the attached Declaration of Robert J. Temple, M.D. make clear, FDA previously reviewed in

107

depth Paxil's side effects and concluded that the drug is, in fact, not habit forming. Thus, the advertisement in question -- also reviewed by the FDA -- is not misleading. As a legal matter, the government also respectfully requests that this Court reject Plaintiffs' injunctive request for the following reasons: 1) FDA's administration of the comprehensive statutory and regulatory scheme governing prescription drug advertising preempts this action; and 2) given the intent of Congress to centralize prescription drug advertisement regulation in the FDA, this Court should defer to the agency's primary jurisdiction.

I. Factual statements

A. Comprehensive regulatory scheme

Congress has charged the United States Secretary of Health and Human Services with regulating drugs marketed in the United States, including the approval, promotion, and labeling of those drugs. See the Federal Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. § 301, et seq. The Secretary has delegated that authority to FDA. 21 C.F.R. § 5.10(a)(1). The comprehensive system of regulation overseen by FDA includes requirements that drug labeling and drug advertisements not be false or misleading. 21 U.S.C. § 352(a), (n); 21 C.F.R. § 202.1(e)(6). Specific regulations state exactly what constitutes a misleading prescription drug advertisement. See, e.g., 21 C.F.R. 202.1(e)(6), (7). If a drug manufacturer publishes false or misleading advertising, the prescription drug is deemed "misbranded," 21 U.S.C. § 352(n), and the United States may bring an enforcement action against the manufacturer. 21 U.S.C. §§

332, 334, 337. There is no private cause of action under the FDCA, 21 U.S.C. § 337(a).

Pursuant to this system of regulation, the FDA's Division of Drug Marketing, Advertising, and Communications ("DDMAC") reviews current broadcast and print prescription drug advertisements appearing in the marketplace for possible enforcement action. Declaration of Robert J. Temple, M.D. ("Decl.") at ¶ 4 (attached hereto). Pursuant to 21 C.F.R. 202.1(j)(4), FDA is committed to review proposed prescription drug advertisements when requested to do so by pharmaceutical companies. FDA's careful examination of regional and nationwide advertisements is designed to ensure that information communicated to consumers is not false or misleading, presents a fair balance of the risks and benefits, reveals material facts, and discloses major side effects. *Id* FDA must consider not only whether adequate information of any risks is disclosed, but also whether such information is presented in such a way that does not overemphasize dangers such that useful drugs are unnecessarily avoided by consumers.

B. FDA's review of the specific advertisements in question

Paxil, the prescription drug at issue in the present case, belongs to a class of pharmaceuticals known as Selective Serotonin Re-uptake Inhibitors (SSRIs). FDA scientists do not consider SSRIs to be habit-forming, as that term has been used in countless drug labels and advertisements. Decl. at ¶ 5. Rather, SSRIs, as well as other kinds of drugs, have been known to cause withdrawal symptoms known as a "discontinuation syndrome." There is a critical difference between this phenomenon and the drug-seeking behavior associated with habit-forming drugs. Decl. at

¶ 6. At the time FDA approved the New Drug Application ("NDA") for Paxil, the agency found no clinical evidence of drug-seeking behavior associated with the use of the drug. Decl. at ¶ 5. In short, FDA concluded that Paxil was not habit forming. Id.

FDA reviewed Paxil advertisements on five separate occasions between 2001 and 2002. Id. Four versions of these advertisements contained the statement "Paxil is non-habit forming." Id. FDA found none of these advertisements to be misleading. Id. The most recent version of the advertisement reviewed by FDA, which Plaintiffs seek to alter, contains the "non-habit forming" language and, additionally, states "Don't stop taking Paxil before talking with your Doctor." Decl. at ¶ 7. FDA concluded upon its review of the current advertisement that the additional precautionary statement to see a doctor regarding discontinuation of the drug ensured that the Paxil advertisement adequately provides for dissemination of information to patients regarding possible SSRI discontinuation symptoms that is contained in the drug's patient package insert. Decl. at ¶¶ 3 and 7. As before, FDA did not consider the advertisement misleading, since it previously had determined that Paxil was not habit forming. Decl. at ¶ 8.

III. Argument

A. Preemption

The Supreme Court has found that:

> Under the Supremacy Clause, the enforcement of a state regulation may be pre-empted by federal law in several circumstances: first, when Congress, in enacting a federal statute, has expressed a clear intent to pre-empt state law; second, when it is clear, despite the absence of explicit preemptive language, that Congress has intended, by legislating comprehensively,

> to occupy an entire field of regulation and has thereby "left no room for the States to supplement" federal law; and, finally, when compliance with both state and federal law is impossible, or when the state law stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress.

Capital Cities Cable, Inc. v. Crisp, 467 U.S. 691, 698-99 (1984) (citations, quotations omitted). While the FDCA lacks an express preemption provision applicable here, Plaintiffs' injunctive request poses an obstacle to the full objectives of Congress by attempting to substitute this Court's judgment for FDA's scientific expertise in determining whether it is misleading to call Paxil "non-habit forming," when it does not create the physical dependency associated with that characterization.

Although some courts have held that certain common law tort actions may escape preemption, a request for specific injunctive relief such as that currently before the Court directly impinges on FDA's role as the protector of the public interest in this field by ordering specific changes to ads that FDA has deemed acceptable. Were the courts of various jurisdictions to mandate what may and may not appear in prescription drug advertisements pursuant to state law, the public undoubtedly would receive inconsistent information from region to region; furthermore, court-imposed advertising content or restrictions would lack the benefit of FDA's scientific expertise and consideration of relevant policy issues. See Weinberger v. Bentex Pharm., Inc., 412 U.S. 645, 654 (1973) (noting that agency expertise is superior to courts' due to "specialization, insight gained through experience, and by more flexible procedures").

In enacting the FDCA, Congress clearly desired that the full range of scientific and medical opinion be brought to bear on the question of publicly available prescription drug information. See 21 U.S.C. § 393(b)(4) (FDA should attempt to carry out its mission "in consultation with experts in science, medicine, and public health, and in cooperation with consumers, users, manufacturers, importers, packers, distributors, and retailers of regulated products."). A regime in which lawsuits motivated by individual, local concerns (even though sincere) may overrule FDA's considered actions in its own defined area of expertise clearly poses an obstacle to the full accomplishment Congressional objectives.

In the present case, FDA reviewed the particular advertisement at issue and made suggestions as to the precise issue that is the subject of plaintiff's request for relief. Based on its scientific and medical expertise with this drug and other similar drugs, FDA decided that the advertisements are acceptable. Under such circumstances, the Court should consider Plaintiffs' purportedly state-law based injunctive request preempted by federal law.[1]

---

[1]Plaintiffs claim to be acting under state law. There is no private right of action under the FDCA. 21 U.S.C. § 337(a). To the extent Plaintiffs' injunctive request "stray[s] too close to the exclusive enforcement domain of the FDA," it must be dismissed. Summit Technology, Inc. v. High-Line Med. Instruments Co., Inc., 922 F.Supp. 299, 306 (C.D.Cal. 1996); see also PDK Labs, Inc. v. Friedlander, 103 F.3d 1105 (2d Cir. 1997) (Plaintiff found to have no standing to challenge retail advertising of a product on the market); Gile v. Optical Radiation Corp., 22 F.3d 540, 544 (3d Cir.1994) (no private right of action under FDCA); Mylan Lab., Inc. v. Matkari, 7 F.3d 1130, 1139 (4th Cir.1993) (dismissing for failure to state a claim plaintiff's "ingenious" attempt to "use the Lanham Act as a vehicle by which to enforce the" FDCA).

B. Primary jurisdiction

Even when common-law rights and remedies survive and the administrative agency lacks the power to confer immunity from a private suit, it may be appropriate to refer specific issues to an agency for initial determination where that procedure would secure "(u)niformity and consistency in the regulation of business entrusted to a particular agency." Nader v. Allegheny Airlines, Inc., 426 U.S. 290, 303-304 (1976). If Plaintiffs are found to state a valid claim despite preemption analysis, the Court should exercise its discretion under the doctrine of primary jurisdiction and allow FDA to consider further, in light of Plaintiffs' arguments, whether the Paxil advertisement is misleading. See Bernhardt v. Pfizer, 2000 WL 1738645 (S.D.N.Y., Nov. 22, 2000) (finding FDA had primary jurisdiction over whether to issue notices to users of prescription drug and their physicians).

The Ninth Circuit noted in United States v. General Dynamics Corp., 828 F.2d 1356 (9th Cir. 1987) that primary jurisdiction "applies when 'protection of the integrity of a regulatory scheme dictates preliminary resort to the agency which administers the scheme.'" Id. at 1362 (quoting United States v. Philadelphia Nat'l Bank, 374 U.S. 321, 353 (1963)); see also United States v. Western Pacific R.R. Co., 352 U.S. 59, 63-4 (1956) (primary jurisdiction applies where "enforcement of the claim requires the resolution of issues which, under a regulatory scheme, have been placed within the special competence of an administrative body"). General Dynamics established four factors that point to a proper invocation of the primary jurisdiction doctrine: "(1) the need to

resolve an issue that (2) has been placed by Congress within the jurisdiction of an administrative body having regulatory authority (3) pursuant to a statute that subjects an industry or activity to a comprehensive regulatory scheme that (4) requires expertise or uniformity in administration." Id. at 1362.

Here, the factors weigh heavily in favor of deferring to FDA. First, Congress clearly intended the FDA to regulate prescription drug marketing. The law gives FDA the authority to review all published prescription drug advertisements and to bring enforcement actions against those who would attempt to mislead the public in any way. The FDCA and its implementing regulations[2] set specific criteria by which the FDA is to judge such advertisements. Second, as set out above, the FDCA subjects the drug industry to a comprehensive national regulatory scheme in which FDA stands at the center. Third, the determination of questions arising under the FDCA - in this case, whether particular drugs may truthfully be described as habit forming or not habit forming - requires both medical and scientific expertise. Moreover, a rational policy requires uniform answers to technical prescription drug questions rather than 50 or more different answers depending on where a consumer happens to live.

While this Court certainly has the authority to interpret the legal meaning of any statute, whether the Paxil advertisement is "misleading" does not present a purely legal question. A factual determination must be made as to whether Paxil truly is

---

[2]The FDCA expressly provides FDA with "[t]he authority to promulgate regulations for the efficient enforcement of the Act." 21 U.S.C. § 371(a).

"habit-forming." This factual review, if undertaken by the Court, "would deny [FDA] the full opportunity to apply its expertise and to correct errors or modify positions in the course of a proceeding." Estee Lauder, Inc. v. FDA, 727 F.Supp. 1, 4 (D.D.C. 1989).[3]

Even if the Court does not agree that it should defer to FDA's determination that the advertisement is not misleading, the agency's position should, at the very least, be "entitled to respect." Christensen v. Harris County, 529 U.S. 576, 587 (2000) (agency interpretations contained in formats such as opinion letters are entitled to respect to the extent they have the power to persuade). FDA doctors and scientists have weighed the concerns at issue in the instant case and have determined the correct balance between alerting the public to the risks of this particular class of drugs and imposing warning requirements that would overly deter use of a life-improving medication. See Henley v. FDA, 77 F.3d 616, 621 (2d Cir. 1996) ("The FDA possesses the requisite know-how to ... sift[] through the scientific evidence to determine the most accurate and up-to-date information regarding a particular drug."). Not only does FDA make such decisions every day across a wide spectrum of drugs, the agency used its particular expertise here to decide whether this specific drug should be categorized as "habit-forming." Given FDA's role under the law and its Congressionally recognized

[3]This is not to say that FDA has not already determined the "non-habit forming" nature of Paxil, but simply to say that, if Plaintiffs have additional information regarding the issue, it should be submitted, in the first instance, to FDA rather than the Courts.

expertise in the area of prescription drugs, this Court should respect the agency's determinations as to both fact and policy

III. Conclusion

The injunction Plaintiffs seek would overrule a factual determination made by FDA in its role as the agency responsible for answering scientific and policy questions in the national arena of prescription drug advertisements. Congress's comprehensive statutory scheme, as implemented by FDA's regulations governing prescription drug advertising, preempts Plaintiff's request. If this Court finds that Plaintiffs' claim is not preempted, it should defer to FDA's considered, expert

determination or, at the very least, refer the matter to FDA in respect of the agency's primary jurisdiction.

Respectfully submitted,

ROBERT D. MCCALLUM, JR.
Assistant Attorney General
Civil Division
EUGENE M. THIROLF
Director
Office of Consumer Litigation

GERALD C. KELL
Senior Trial Counsel
Office of Consumer Litigation
U.S. Department of Justice
P.O. Box 386
Washington, D.C. 20044
Tel: (202) 514-1586

ALAN PHELPS
Trial Attorney
Office of Consumer Litigation
U.S. Department of Justice
P.O. Box 386
Washington, D.C. 20044
Tel: (202) 307-6154

OF COUNSEL:

DANIEL E. TROY
Chief Counsel

ERIC M. BLUMBERG
Deputy Chief Counsel

CARL I. TURNER
Associate Chief Counsel
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

ROBERT D. MCCALLUM, JR.
Assistant Attorney General
Civil Division
EUGENE M. THIROLF
Director
Office of Consumer Litigation
GERALD C. KELL
Senior Trial Counsel
Office of Consumer Litigation
ALAN PHELPS
Trial Attorney
U.S. Department of Justice
P.O. Box 386
Washington, D.C. 20044
(202) 307-6154

Attorneys for the United States

UNITED STATES DISTRICT COURT
FOR THE CENTRAL DISTRICT OF CALIFORNIA

IN RE PAXIL LITIGATION	CV-01-07937 MRP (CWx)
THIS DOCUMENT RELATES TO ALL ACTIONS	DECLARATION OF ROBERT J. TEMPLE, M.D.

I, Robert J. Temple, M.D., declare as follows:

1. I hold two positions within the Food and Drug Administration's ("FDA") Center for Drug Evaluation and Research ("CDER"): I am the Director of the Office of Medical Policy and the Acting Director of the Office of Drug Evaluation I ("ODE-I"). I have held these or similar positions since 1982. My office is located at 1452 Rockville Pike, Rockville, Maryland.

2. ODE-I is staffed with physicians and scientists responsible for the regulation of cardio-renal, oncologic, and neuropharmacologic/psychopharmacologic drug products. My office decides whether to approve new drug applications ("NDAs") for these types of drug

products. Under the laws FDA administers, NDAs must include proposed drug product labeling. I personally make decisions on the approvability of NDAs for all new molecular entities for the above types of drug products. In the course of my official duties, I reviewed and approved the drug Paxil and its product labeling. Paxil is a neuropharmacologic/psychopharmacologic drug.

3. In addition to reviewing labeling prior to a drug's approval, once an approved drug product has been marketed, ODE-1, in conjunction with CDER's Office of Drug Safety, monitors the frequency and severity of postmarketing adverse events to determine whether labeling changes are necessary or warranted. The Paxil labeling (package insert) has been periodically revised both as to new indications that have been approved (e.g., post-traumatic stress disorder) and in response to postmarketing adverse event reports. For instance, based on limited data, the April 13, 2001 Paxil package insert that accompanied the approval letter for the generalized anxiety disorder indication included minor comments in the Postmarketing Reports paragraph of the ADVERSE REACTIONS section signaling a potential problem with "discontinuation syndrome." By December 14, 2001, with more data in hand, the Paxil package insert, this time attached to the approval letter for the another (post-traumatic stress disorder) indication, was revised to reflect additional reports of discontinuation syndrome as an associated risk of taking the drug. The labeling change moved the description of the syndrome from the ADVERSE REACTIONS section/Postmarketing Reports to a new paragraph captioned PRECAUTIONS Section/Discontinuation of Treatment with Paxil. The following language regarding discontinuation syndrome was included (final printed label issuance date, Jan. 2002):

> ...[t]he following adverse events were reported at an incidence of 2% or greater for *Paxil* and were at least twice that reported for placebo: abnormal dreams (2.3% vs. 0.5%), paresthesia (2.0% vs. 0.4%), and dizziness (7/1% vs. 1.5%). In the majority of patients, these events were mild to moderate and were self-limiting and did not require medical intervention.
>
> During *Paxil* marketing, there have been spontaneous reports of similar adverse events, which may have no causal relationship to the drug, upon the discontinuation of *Paxil* (particularly when abrupt), including the following: dizziness, sensory disturbances, (e.g., paresthesias, such as electric shock sensations), agitation, anxiety, nausea, and sweating. These events are generally

self-limiting. Similar events have been reported for other selective serotonin reuptake inhibitors.

Patients should be monitored for these symptoms when discontinuing treatment, regardless of the indication for which *Paxil* is being prescribed. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose but at a more gradual rate (See DOSAGE AND ADMINISTRATION).

4. The Office of Medical Policy is responsible for the regulation of promotion of prescription drug products through the Division of Drug Marketing, Advertising, and Communications ("DDMAC"). DDMAC's mission is to protect the public health by insuring that prescription drug information is truthful, not misleading, balanced, and accurately communicated. DDMAC is responsible for regulating the promotional activities of the prescription drug industry. This includes the review of proposed advertisements when requested to do so by a pharmaceutical company. Pharmaceutical manufacturers often seek DDMAC's review of their proposed television advertisements in advance. Once an advertisement is disseminated, FDA regulations require the company to submit the advertisement to DDMAC. DDMAC reviews advertisements that are currently in use to ascertain compliance with the law. FDA has authority, administered through DDMAC, to regulate the content of prescription drug advertisements printed in magazines, journals, and newspapers; broadcast over television, radio, and telephone; and disseminated through other means. DDMAC reviews these advertisements to ensure that they are not false or misleading (not inconsistent with approved product labeling); present a fair balance between the risks and benefits of a drug product; reveal facts material in light of the consequences of using the product as advertised; and either disclose all the risks associated with use of the product described in the FDA approved product labeling or, for broadcast advertisements, disclose the major risks and make adequate provision for disseminating the product's FDA-approved labeling to the advertisement's audience. As Director of this Office, I am involved in the resolution of complicated issues regarding direct-to-consumer

advertising. DDMAC conducted a review of the television advertising for the drug Paxil that is the subject of this litigation and I am familiar with its decisions and actions.

5. During the period May 2001 through June 2002, DDMAC reviewed the contents of defendant's television advertisements for Paxil on five separate occasions: May 18, 2001, August 22, 2001; September 26, 2001; April 29, 2002; and June 14, 2002. DDMAC provided comments to the manufacturer on three of these occasions, in letters dated May 18, 2001, August 22, 2001, and April 29, 2002. See attachments 1-5. The last four versions of these television advertisements included the oral statement that "Paxil is non-habit forming." The last and current version of the advertisement contains the statement, "Don't stop taking Paxil before talking with your Doctor." Although on these occasions DDMAC commented on other aspects of the advertisements, at no time did DDMAC conclude that the statement "Paxil is non-habit forming" was misleading. The reason for this is that DDMAC was aware that the medical reviewers and scientists at ODE-I had already determined during their medical and scientific review of the NDA for Paxil that there was no clinical evidence of drug-seeking behavior associated with the use of Paxil. Given the lack of any scientific evidence in the NDA suggestive of drug abuse potential for Paxil, and its membership in a class of drugs not suspected of having abuse potential (selective serotonin reuptake inhibitors), there was no reason for ODE-I to consider the drug to be habit forming. "Habit forming" is not a scientifically precise term, but generally implies that patients will seek out the drug and continue to take it in the absence of a medical need. A term used more widely would be that the drug has "abuse potential." If ODE-I had considered Paxil to be potentially habit forming, it would have referred the matter to the United States Drug Enforcement Agency for possible scheduling under the Controlled Substances Act, which it decided was unnecessary. Based on this, DDMAC concluded that the statement "Paxil is non-habit forming" was not misleading.

6. The fact that a drug causes a discontinuation syndrome does not mean that it is a habit forming drug. Discontinuation syndrome generally refers to the emergence of various signs and

symptoms that occur when a drug is stopped abruptly (beyond a simple return of the symptoms the drug was used to treat). In many cases, such syndromes are thought to reflect changes in drug receptors that lead to greater sensitivity to endogenous substances or other influences. There are a number of drugs with unequivocal discontinuation syndromes that FDA and others would not consider to be habit forming. For example, beta blockers, used to treat high blood pressure, have a serious and even dangerous discontinuation syndrome. Clonidine, also used to treat high blood pressure, does as well, as do nitroglycerin and its relatives. None of these drugs is associated with drug seeking behavior or drug abuse. These drugs are in contrast to narcotics, benzodiazepines, amphetamines, and barbiturates, all of which cause both discontinuation syndromes and drug seeking behavior. Some habit forming drugs, such as marijuana, are associated with drug seeking behavior, but do not have discontinuation syndromes.

7. In response to the recent requirement by ODE-I that the labeling for Paxil contain information about symptoms some patients were experiencing when they stopped taking Paxil, the defendant had originally proposed that the "major statement" in their television advertisement include, "Always talk to your doctor before stopping Paxil." On April 29, 2002, DDMAC suggested to the defendant that they strengthen the "major statement" to better convey to consumers what they might experience should they stop taking Paxil. DDMAC suggested that the oral statement be changed to "Don't stop taking Paxil before talking with your Doctor." This addition accompanies the statement, "Paxil is non-habit forming," which was present in this television advertisement as submitted by the defendant for review. DDMAC concluded that putting this precaution into the television advertisements would ensure that the ads adequately provided for dissemination of the information about possible discontinuation symptoms, contained in detail in the product's FDA-approved insert. This method of disseminating information contained in product labeling is consistent with FDA's regulations.

8. In summary, FDA carefully reviewed the contents of defendants' past and current television advertisements for Paxil in this case. The agency concluded that the advertisements were not misleading because there is no scientific evidence that Paxil is a habit forming drug and consumers are adequately cautioned ("Don't stop taking Paxil before talking with your doctor") so that they will be informed about any symptoms they may experience before they stop taking Paxil and will do so under the guidance of their physician.

Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct.

Executed this 4 day of September, 2002.

Robert J. Temple, M.D.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

TRANSMITTED BY FACSIMILE

Thomas Kline
Assistant Director, U.S. Regulatory Affairs
GlaxoSmithKline
1250 South Collegeville Road
P.O. Box 5089
Collegeville, PA 19426-0989

RE: NDA 20-031/S-026
Paxil (paroxetine hydrochloride) Tablets
MACMIS ID#: 9955

Dear Mr. Kline:

This letter responds to GlaxoSmithKline's (GSK) April 17, 2001, letter to the Division of Drug Marketing, Advertising, and Communications (DDMAC), requesting comments on two proposed direct-to-consumer (DTC) broadcast television advertisements for Paxil (paroxetine hydrochloride) Tablets for treatment of generalized anxiety disorder (GAD). The submission included storyboards for two 60 second ads entitled "My Anxiety" and "Misunderstood/What They Face" (labeled storyboards version "A" and "B" respectively).

We have reviewed the proposed materials and offer the following comments.

Storyboards and scripts often fail to account for factors of audio and video production that could affect the effective communication of important information and fulfillment of adequate provision disclosures (e.g., graphics and superimposition of text, pacing and clarity of voiceovers, and sound effects or music). Therefore, we remind you that we cannot provide final comments on the acceptability of the broadcast ads unless we review the final taped version in its entirety.

Since many claims and representations are similar or closely related, our comments on a particular claim or representation should be applied to all future materials for Paxil that contain similar claims and presentations.

Adequate Communication of Complete Indication

Based on the collection of images and language used to describe GAD, the proposed broadcast ads are misleading because the descriptions of the indication fails to adequately convey the hallmark symptoms and the serious nature of the illness in order to sufficiently communicate the intensity of the distress suffered. The totality of the opening vignettes dramatizing people suffering from various symptoms of GAD do not convey the concept that the sufferer finds it difficult to control their chronic symptoms of excessive anxiety, worry, tension, irritability, etc.

Furthermore, the GAD indication in the Paxil approved product labeling (PI) states that anxiety or tension associated with the stress of everyday life usually does not require treatment with an anxiolytic. However in version "A," the message that such everyday anxiety does not usually need medication is not adequately communicated by the statement "feeling anxiety is part of life." We note that based on the storyboard sequence in version "A," the placement of the SUPER "feeling anxiety is part of life" between the GAD vignettes and the clinical definition of GAD undermines communication of the concept of uncontrollability of the symptoms for GAD sufferers.

In addition, in both proposals, the frame featuring SUPERs identifying the variety of symptoms associated with GAD lacks sufficient prominence (either due to font type size, lack of contrast, or possibly inadequate display time). In addition, we recommend revising some of the symptom terminology for accuracy (revise "tension" to "muscle tension") or for more consumer-friendly language (revise "fatigue" to "easily tired" or "excessively tired"). We note that the artwork SUPER for frame 7 in version "B" omits the symptom of fatigue.

Minimization of Risk Information

In both proposals, the presentation minimizes some of the risk information. The statement "People taking MAOIs or thioridazine shouldn't take Paxil" followed by "Side effects may include..." implies that only those people taking either of those drugs would experience the side effects listed if they used Paxil. Therefore, to clarify that any Paxil user might experience the listed side effects we recommend revising the second statement (i.e., "Paxil's side effects include...."). In addition, to be consistent with the PI, we recommend that the side effect disclosure regarding sexual side effects be revised (i.e., "sexual side effects in men and women").

Lack of Prominence for Various SUPERs

In both proposals, various SUPERs ("Available by prescription only" and those to fulfill "Adequate Provision") lack sufficient prominence for readability and processing by the viewer.

SUPER "*The most prescribed SSRI for anxiety*" (*version "A"*)

The presentation of this marketing claim in a SUPER during the audio presentation listing the most common side effects minimizes communication of this risk information. We recommend presenting this claim elsewhere. In addition, for easier comprehension of the marketing claim, we recommend revising the language to that proposed in version "B", "*the most prescribed medication of its kind for* Generalized Anxiety."

If you have any questions or comments, please direct them to Lisa L. Stockbridge by facsimile at (301) 594-6771, or at the Food and Drug Administration, Division of Drug Marketing, Advertising, and Communications, HFD-42, Rm 17-B-20, 5600 Fishers Lane, Rockville, MD 20857. DDMAC reminds GSK that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID# 9955 in addition to the NDA number.

Sincerely,

{See appended electronic signature page}

Joan Hankin, JD
Consumer Promotion Analyst
Division of Drug Marketing,
Advertising, and Communications

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Joan Hankin
5/18/01 10:27:24 AM

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville, MD 20857

TRANSMITTED BY FACSIMILE

Thomas Kline
Assistant Director, U.S. Regulatory Affairs
GlaxoSmithKline
1250 South Collegeville Road
P.O. Box 5089
Collegeville, PA 19426-0989

RE: NDA 20-031/S-026
Paxil (paroxetine hydrochloride) Tablets
MACMIS ID#: 9955

Dear Mr. Kline:

This letter responds to GlaxoSmithKline's (GSK) August 1, 2001, request to the Division of Drug Marketing, Advertising, and Communications (DDMAC) for comments on two revised proposed direct-to-consumer (DTC) broadcast television advertisements for Paxil (paroxetine hydrochloride) Tablets for treatment of generalized anxiety disorder (GAD). The submission included storyboards and videotapes for two 60 second ads entitled "My Anxiety"/GXPX-1006 and "What They Face"/GXPX-1016.

We have reviewed the proposed materials and offer the following comments. Since many claims and representations are similar or closely related, our comments on a particular claim or representation should be applied to all future materials for Paxil that contain similar claims and presentations and should be communicated in consumer-friendly language.

Adequate Communication of Indication Limitation

As discussed in our May 18, 2001, letter, the GAD indication in the Paxil approved product labeling (PI) states that anxiety or tension associated with the stress of everyday life usually does not require treatment with an anxiolytic. We commented that this message (that such everyday anxiety does not usually need medication) would not be adequately communicated by "feeling anxiety is part of life." We also noted that based on the storyboard sequence in version "My Anxiety," the placement of the SUPER "feeling anxiety is part of life" undermined communication of the concept of uncontrollability of the symptoms for GAD sufferers.

You responded by deleting the statement "feeling anxiety is part of life," but you did not suggest any revised language to expressly articulate this limitation to the indication. We seek to clarify our comment. To accurately communicate the complete indication and avoid inappropriately expanding the patient population, we recommend adding information to clearly convey the concept that anxiety due to the stresses of everyday life usually does not require medication.

Thomas Kline
GlaxoSmithKline
NDA 20-031

Minimization of Risk Information

We have reviewed your response and would not object to your revised proposal.

If you have any questions or comments, please direct them to Lisa L. Stockbridge by facsimile at (301) 594-6771, or at the Food and Drug Administration, Division of Drug Marketing, Advertising, and Communications, HFD-42, Rm 17-B-20, 5600 Fishers Lane, Rockville, MD 20857. DDMAC reminds GSK that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID# 9955 in addition to the NDA number.

Sincerely,

{See appended electronic signature page}

Joan Hankin, JD
Consumer Promotion Analyst
Division of Drug Marketing,
Advertising, and Communications

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/
Joan Hankin
8/22/01 11:07:38 AM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

TRANSMITTED BY FACSIMILE

Thomas Kline
Director, Regulatory Affairs
GlaxoSmithKline
1250 South Collegeville Road
P.O. Box 5089
Collegeville, PA 19426-0989

RE: NDA #20-031
Paxil (paroxetine HCl) Tablets
MACMIS #10828

Dear Mr. Kline:

This letter is in response to your April 5, 2002, request to the Division of Drug Marketing, Advertising, and Communications (DDMAC) for comments on a proposed direct-to-consumer (DTC) broadcast advertisement regarding the generalized anxiety disorder (GAD) indication for Paxil (paroxetine HCL) Tablets. Your submission includes a storyboard and a 60-second video entitled "My Anxiety."

DDMAC has reviewed the proposed materials and has the following comments:

1. The claim "I like my life again" (Frame 14) is misleading because it broadly implies that Paxil can improve anyone's life, to the extent that they will like their life, when this has not been demonstrated by substantial evidence from adequate and well-controlled clinical trials using validated instruments that are designed to measure the patient's appreciation for life.

2. DDMAC is concerned that the claim "Always talk to your doctor before stopping Paxil" does not convey the importance of the Precaution, in the approved product labeling, regarding the potential risk of abrupt discontinuation of Paxil and the need to consult a physician before doing so. Thus, DDMAC suggests that the directive be given more impact. For example, "Do not stop taking Paxil before talking with your doctor."

If you have any questions or comments, please contact me by facsimile at (301) 594-6771, or at the Food and Drug Administration, Division of Drug Marketing, Advertising, and Communications, HFD-42, Rm. 17B-20, 5600 Fishers Lane, Rockville, MD 20857. DDMAC reminds you that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID #10828 in addition to the NDA number.

Sincerely,

(See appended electronic signature page)

Lisa L. Stockbridge, Ph.D.
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/
Lisa Stockbridge
4/29/02 10:52:17 AM

c.233 7/1/01

"My Anxiety" :60 ISCI: GXPX-1006 (Newsweek)

DIRECTOR'S NOTE: This commercial features 'real people' (i.e., not actors) who have been screened as sufferers of Generalized Anxiety Disorder. The film will be clips of interviews with these sufferers, where they have talked about their excessive and persistent anxiety, worry and tension, how it feels, how they would describe it, and how it has impacted them, all in their own words. There are no special effects. The music during the vignettes has been designed to underscore and help dramatize the persistent and severe nature of chronic anxiety.

Frame 1
The spot opens on the first sufferer, who talks about how her anxiety is always with her.

Director's note: The message conveyed by this sufferer is the chronic nature of her anxiety and her inability to manage it.

Raven V/O
I'm always thinking something terrible is going to happen. I can't handle it.

Frame 2
Cut to a second sufferer, talking about the persistency of her anxiety and tension. Her body language and facial expression reflect the severity of her chronic anxiety.

Director's note: The message to be conveyed by this sufferer is her distress about her lack of control over her worry.

Rosemary V/O:
You know ...your worst fears, you know, that what if's...and I can't control it and I'm always worrying about everything.

Frame 3
Cut to third sufferer who is very candidly discussing her chronic anxiety and the fact that she used to think it was part of her personality.

Director's Note: The message conveyed here is the persistency of her worry and that she used to not know it was something treatable.

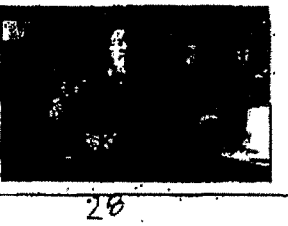
Susannah V/O:
It's like a tape in my mind. That list goes over, and over, and over. I just thought I was a worrier.

Frame 4
Cut to title card and PAXIL logo.

TITLE CARD:
The real story about chronic anxiety

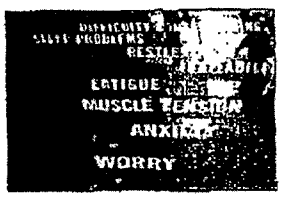
Frame 5
Cut to fourth sufferer, sitting in a chair talking about his constant anxiety and tension.

Director's Note: The message this sufferer conveys is the inability to control his worry, anxiety and tension.



Russell V/O:
It's like I never get a chance to relax – At work, I'm tense about stuff at home. At home, I'm tense about stuff at work.

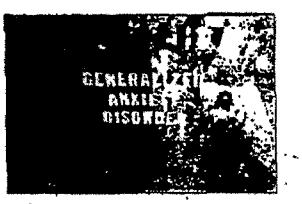
Frame 6
Cut to a shot of many people walking. Supers appear over the scene which are hallmark symptoms of GAD, as well as physical symptoms that can be associated with GAD – "worry," "anxiety," "muscle tension," "fatigue," "irritability," "restlessness," "sleep problems," "difficulty concentrating."



AVO
If you're one of the millions of people who live with uncontrollable worry, anxiety, and several of these symptoms for 6 months or more,

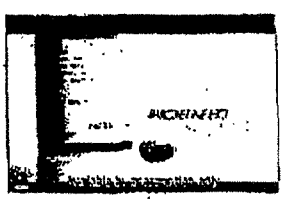
(Reference: Indication section of prescribing information)

Frame 7
The individual words blend together through a camera technique and become a super which says "Generalized Anxiety Disorder."



you could be suffering from Generalized Anxiety Disorder and a chemical imbalance could be to blame

Frame 8
Cut to a product shot of a prescription bottle and a single Paxil pill, along with the Paxil logo. A super appears which says "Available by prescription only."



Paxil works to correct this imbalance to relieve anxiety

Frames 9-13
Cut to shots of the people from frames 1-5 returning to their daily activities.

Super:
Anxiety from everyday stresses usually doesn't need medication.

AVO - FAIR BALANCE:
Prescription Paxil is not for everyone.

Frame 10
Super:
For more information talk to your doctor.

Frame 11
Super: "See our ad in Newsweek"

Tell your doctors what medicines you're taking

Frame 12
Supers: "1-800-20PAXIL"
"www.paxil.com"

Frame 13
Supers: "1-800-20PAXIL"
"www.paxil.com"

Side effects may include decreased appetite, dry mouth, sweating, nausea, constipation, sexual side effects, tremor, fatigue, or sleepiness. People taking MAOIs or thioridazine should not take Paxil.

(Reference: Adverse reactions & contraindications section of labeling)

Paxil is non-habit forming.

Frame 14
Cut to the first sufferer who has been relieved through treatment, and is describing how worry no longer consumes her, she's regained some normalcy in her life.

The Paxil logo appears

Person V/O.
I'm not bogged down by worry anymore. I feel like me again.... I feel like myself.

Frame 15
The tag line fades up "Your life is waiting."

Super:
Paxil.
Your life is waiting

80

Note: Form 2253 is required by law. Reports are required for approved NDAs and AbDAs (21 CFR 314.81)

TRANSMITTAL OF ADVERTISEMENTS AND PROMOTIONAL LABELING FOR DRUGS AND BIOLOGICS FOR HUMAN USE

1. DATE SUBMITTED: September 14, 2001

2. LABEL REVIEW NO. (Biologics): 115916

Form Approved: OMB No. 0910-0376
Expiration Date: August 31, 2001
See OMB Statement on Reverse of Form

3. NDA/ANDA/AADA OR BLA/PLA/PMA Number: 20-031
Single product: ☑ Multiple products: ☐
For multiple products, submit completed form and specimen of advertising/promotional materials to one application of choice, and attach separate sheet addressing items 3-5 for remainder of products. Refer to No. 3 on instruction sheet

4. PROPRIETARY NAME	5. ESTABLISHED NAME (Prod. Code No)	6. PACKAGE INSERT DATE and ID NO (Latest final printed labeling)	7. MANUFACTURER NAME: (License No (Biologics))
Paxil (Tablets)	paroxetine hydrochloride	PX:L20, April 2001	SmithKline Beecham Pharmaceuticals

FDA/CBER USE ONLY

REVIEWED BY:	DATE	RETURNED BY:	DATE

8. ADVERTISEMENT / PROMOTIONAL LABELING MATERIALS

Material Type (use FDA codes) a.	Dissemination/ Publication Date b.	Applicant's Material ID Code and/or description c.	Previous review No. if applicable / date (PCA Submissions) d.	COMMENTS
CTV	Sept. 2001	GXPX-1006 - Video and Storyboard for reviewer convenience		
CTV	Sept. 2001	GXPX- 1016 - Video and Storyboard for reviewer convenience		

9. TYPED NAME AND TITLE OF RESPONSIBLE OFFICIAL OR AGENT
Thomas Kline
Assistant Director, U.S. Regulatory Affairs

10. SIGNATURE OF RESPONSIBLE OFFICIAL

11. APPLICANT'S RETURN ADDRESS
SmithKline Beecham Pharmaceuticals
Mail Code UP4340
1250 South Collegeville Road
PO Box 5089
Collegeville, PA 19426-0989

12. RESPONSIBLE OFFICIAL'S
a. PHONE NO. (610) 917-5570
b. FAX NO. (610) 917-7985

CENTER FOR DRUG EVALUATION AND RESEARCH RECD SEP 17 2001 DDMAC

13. BIOLOGICAL PRODUCTS. (Check one)
☐ Part I (Draft) ☐ Part II (Final)

FORM FDA 2253 (8/98) PREVIOUS EDITION IS OBSOLETE.

Hankin, Joan E

From: Stockbridge, Lisa L
Sent: Thursday, September 27, 2001 10:12 AM
To: Hankin, Joan E
Subject: RE: Paxil 2253 TV Tapes

Thanks for taking care of this. I don't have to see the tapes.

Lisa

-----Original Message-----
From: Hankin, Joan E
Sent: Wednesday, September 26, 2001 1:51 PM
To: Stockbridge, Lisa L
Subject: Paxil 2253 TV Tapes

Lisa:

I reviewed the tapes "My Anxiety" and "What They Face" and they addressed our only comment from 8/22 to replace language for the indication limitation. They now have a sustained SUPER that says "Anxiety from everyday stresses usually doesn't need medication."

Let me know if you want to view the tapes for signoff before I put them on the shelf.

Thanks,

Joan

AdHIS FDA2253 CONTROL FORM
17-SEP-2001

2253 ID: 115918 Reviewer: STOCKBRIDGE, LISA

NDA No: N020031
Drug: PAXIL (PAROXETINE HCL) TABLETS
Pharm: 2020300
Div: 120
Sponsor: SKB PHARMS

Submiss Date: 14-SEP-2001
Receipt Date: 17-SEP-2001
Pkg Insert Date:
Pkg Insert ID:
Date to Rev: 17-SEP-2001

Single/Multi Mar: S
Number of NDAs: 1

Incomplete Package Codes

No incomplete package codes for this FDA2253

Advertisement/Promotional Labeling Material

Issue Date	Material ID	Type	Description	Aud
01-SEP-2001	GXPX10006	CVT	MY ANXIETY. :60	
01-SEP-2001	GXPX1016	CVT	WHAT THEY FACE. :60	

Agent Name: THOMAS KLINE, ASST DIR.
Company: SMITHKLINE BEECHAM
Street: 1250 SOUTH COLLEGEVILLE RD UP4455
City: COLLEGEVILLE
State: PA
Zip: 194260989

Review Categories

Review Type	Material ID	Category Criteria	Selection Criteria

No Priority Review Categories for this FDA2253 ID #

Subject to communicate limitation to Indication
"Anxiety from everyday stresses usually doesn't need medication."

dlc jch 9/26/01

2253 6/12/02

"My Anxiety" :60 Refresh GXPX-2006

DIRECTOR'S NOTE: This commercial features "real people" (i.e., not actors) who have been screened as sufferers of Generalized Anxiety Disorder. The film will be clips of interviews with these sufferers, where they have talked about their excessive and persistent anxiety, worry and tension, how it feels, how they would describe it, and how it has impacted them, all in their own words. There are no special effects. The music during the vignettes has been designed to underscore and help dramatize the persistent and severe nature of chronic anxiety.

Frame 1
The spot opens on the first sufferer, who talks about how her anxiety is always with her, so much that she can't fully take part in her life.

Director's note: The message conveyed by this sufferer is the chronic nature of her anxiety and her inability to manage it.

Steward VO.
It's like I can't participate in life. I'm too busy worrying. I don't sleep at night. I'm thinking about my friends, I'm thinking about my family...

Frame 2
Cut to a second sufferer, talking about the persistency of her anxiety and tension. Her body language and facial expression reflect the severity of her chronic anxiety.

Director's note: The message to be conveyed by this sufferer is her distress about her lack of control over her worry.

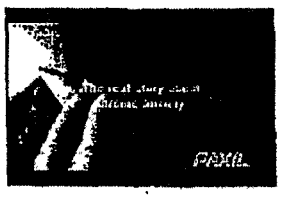
Rosemary VO.
You know .. your worst fears, you know, the what ifs....and I can't control it and I'm always worrying about everything.

Frame 3
Cut to third sufferer who is very candidly discussing her chronic anxiety and the fact that others, who don't suffer, can't understand what she feels like.

Director's Note: The message conveyed here is the persistency of her worry and that she used to not know it was something treatable.

Nicole VO
So no, I don't tell people about my anxiety, everyone thinks I'm overreacting.

Frame 4
Cut to title card and PAXIL logo.



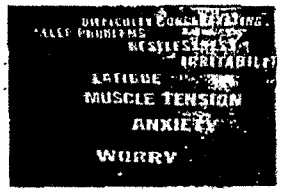
TITLE CARD:
The real story about chronic anxiety

Frame 5
Cut to fourth sufferer, sitting in a chair talking about his constant anxiety and tension.

Director's Note: The message the sufferer conveys is the inability to control his worry, anxiety and tension.

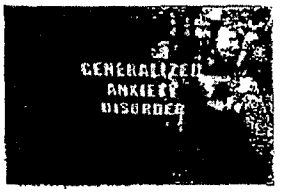
Russell VO.
It's like I never get a chance to relax – At work, I'm tense about stuff at home At home, I'm tense about stuff at work

Frame 6
Cut to a shot of many people walking. Supers appear over the scene which are hallmark symptoms of GAD, as well as physical symptoms that can be associated with GAD – "worry," "anxiety," "muscle tension," "fatigue," "irritability," "restlessness," "sleep problems," "difficulty concentrating."



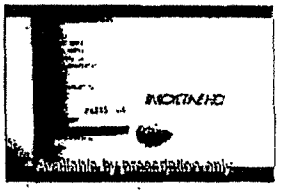
AVO:
If you're one of the millions of people who live with uncontrollable worry, anxiety and several of these symptoms for 6 months or more

Frame 7
The individual words blend together through a camera technique and become a super which says "Generalized Anxiety Disorder."



you could be suffering from Generalized Anxiety Disorder and a chemical imbalance could be to blame.

Frame 8
Cut to a product shot of a prescription bottle and a single Paxil pill, along with the Paxil logo. A super appears which says "Available by prescription only."



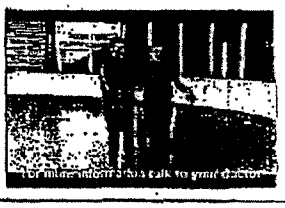
Paxil works to correct this imbalance to relieve anxiety.

Frames 9-13
Cut to shots of the people from frames 1-5 returning to their daily activities.

Super:
Anxiety from everyday stresses usually doesn't need medication.

AVO - FAIR BALANCE
Prescription Paxil is not for everyone

Frame 10
Super:
For more information talk to your doctor.



Frame 11
Super: "Site our ad in Marie Claire"

Tell your doctors what medicines you're taking

Frame 12
Subers: "1-800-20PAXIL"
"www.paxil.com"

Frame 13
Subers: "1-800-20PAXIL"
"www.paxil.com"

Side effects may include decreased appetite, dry mouth, sweating, nausea, constipation, sexual side effects, tremor, fatigue, or sleepiness. Don't stop taking Paxil before talking with your doctor. People taking MAOIs or thioridazine should not take Paxil.

Paxil is non-habit forming

Frame 14
Cut to the first sufferer who has been relieved through treatment, and is describing how worry no longer consumes her; she's regained some normalcy in her life.

The Paxil logo appears.

Steward V/O.
Facing the day is easier... I feel like me again.

Frame 15
The tag line fades up "Your life is waiting."

Super
Paxil.
Your life is waiting

Note: Form 2253 is required by law. Reports are required for approved NDAs and ANDAs (21 CFR 314.81)

TRANSMITTAL OF ADVERTISEMENTS AND PROMOTIONAL LABELING FOR DRUGS AND BIOLOGICS FOR HUMAN USE

Form Approved: OMB No. 0910-0297
Expiration Date: August 31, 2001
See OMB Statement on Reverse of Form

1 DATE SUBMITTED: 12 June 2002

2 LABEL REVIEW NO (if applicable): 126770 S-1

3 NDA/ANDA/PMA/PDA OR IND/APL/APMA
Number: 20-031
Single product: ☑ Multiple products: ☐
For multiple products, submit completed form and specimen of advertising/promotional materials to the application or docket, and attach separate sheet addressing items 3-5 for remainder of products. Refer to No. 3 on instruction sheet.

4 PROPRIETARY NAME	5 ESTABLISHED NAME	6 PACKAGE INSERT DATE and ID NO (Latest final printed labeling)	7 MANUFACTURER NAME
Paxil (Tablets)	paroxetine hydrochloride Prod Code No	January 2002, PX-L22	SmithKline Pharmaceutical Puerto Rico Inc License No (if applicable) d/b/a GlaxoSmithKline

FDA/CBER USE ONLY

REVIEWED BY	DATE	RETURNED BY	DATE

8 ADVERTISEMENT / PROMOTIONAL LABELING MATERIALS

Material Type (use FDA codes) a	Dissemination/ Publication Date b	Applicant's Material ID Code and/or description c	Previous Review No if applicable / date (PDA Submissions) d	COMMENTS
CTV	June 2002	"My Anxiety" Video tape and Storyboard(GXPX-2006)		

9 TYPED NAME AND TITLE OF RESPONSIBLE OFFICIAL OR AGENT
Thomas F. Kline
Director, U.S. Regulatory Affairs

10 SIGNATURE OF RESPONSIBLE OFFICIAL
Mobbi Wilson for T. Kline

11 APPLICANT'S RETURN ADDRESS
GlaxoSmithKline
Mail Code UP4340
1250 South Collegeville Road
PO Box 5089
Collegeville, PA 19426-0989

12 RESPONSIBLE OFFICIAL'S
a PHONE NO: (610) 917-5970
c FAX NO: (610) 917-7666

RECEIVED
JUN 13 2002
DDMAC / CDER

13 BIOLOGICAL PRODUCTS: (Check one)
☐ Part I Draft ☐ Part II Final

FORM FDA 2253 (8/98) PREVIOUS EDITION IS OBSOLETE

AcNIS FDA2253 CONTROL FORM
13-JUN-2002

2253 ID: 126770 Reviewer: STOCKBRIDGE, LISA

NDA No: N020031 Submiss Date: 12-JUN-2002 Single/Multi Mat: S
Drug: PAXIL (PAROXETINE HCL) TABLETS Receipt Date: 13-JUN-2002 Number of NDAs: 1
Pharm: 2020100 Pkg Insert Date:
Div: 120 Pkg Insert ID:
Sponsor: GLAXOSMITHKLINE Date to Rev: 13-JUN-2002

Incomplete Package Codes

No incomplete package codes for this FDA2253

Advertisement/Promotional Labeling Material

Issue Date	Material ID	Type	Description	Aud
01-JUN-2002	GXPX2006	CIV	MY ANXIETY./Refresh	

Agent Name: THOMAS F.KLEINE,DIR.
Company: GLAXOSMITHKLINE
Street: 1250 SOUTH COLLEGEVILLE RD
City: COLLEGEVILLE
State: PA Zip: 194260969

Review Categories

Review Type	Material ID	Category Criteria	Selection Criteria

No Priority Review Categories for this FDA2253 ID #

:60 "My Anxiety - Refresh"

olujeh 6/14/02

30

09/13/02 18:19 FAX

039

CERTIFICATE OF SERVICE

I certify that on September 4, 2002, I served copies of the foregoing Brief of the United States and attached Declaration of Robert J. Temple, M.D., by Federal Express overnight delivery upon counsel listed below:

Karen Barth
Baum Hedlund Aristei Guilford & Schiavo
12100 Wilshire Blvd., Suite 950
Los Angeles, CA 90025
Telephone (310) 207-3233
Facsimile (310) 820-7444

Donald J. Farber
Law Offices of Donald J. Farber
7 Mt. Lassen Drive
Suite D-122
San Rafael, CA 94903
Telephone: (415) 472-7181
Facsimile: (415) 472-7182

Zev B. Zysman
Weiss & Yourman
10940 Wilshire Blvd, 24th Floor
Los Angeles, CA 90024
Telephone: 310-208-2800
Fasimile: 310-209-2348

Mark S. Brown
Ashley Whitesides
King & Spalding
1730 Pennsylvania Avenue, N.W.
Washington, D.C. 20006-4706
Telephone: 202-737-0500
Facsimile: 202-626-3737

Gerald C. Kell

GERALD C. KELL
Senior Trial Counsel
U.S. Department of Justice